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| <b>TRANSMITTAL LETTER TO THE UNITED STATES<br/>DESIGNATED/ELECTED OFFICE (DO/EO/US)<br/>CONCERNING A SUBMISSION UNDER 35 U.S.C. 371</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                         | ATTORNEY'S DOCKET NUMBER<br>0470-045923<br>U.S. APPLICATION NO. (If known, see 37 CFR 1.5)<br><b>10/517688</b> |
| INTERNATIONAL APPLICATION NO.<br>PCT/NL03/00422                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | INTERNATIONAL FILING DATE<br>11.06.2003 (June 11, 2003) | PRIORITY DATE CLAIMED<br>11.06.2002 (June 11, 2002)                                                            |
| TITLE OF INVENTION<br>METHOD OF TREATING OR PREVENTING IMMUNE MEDIATED DISORDERS AND PHARMACUTICAL FORMULATION FOR USE .....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                         |                                                                                                                |
| APPLICANT(S) FOR DO/EO/US<br>Evert Johannes BUNSCHOTEN, Herman Jan Tijmen COELINGH BENNINK, and Christian Franz HOLINKA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                         |                                                                                                                |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                         |                                                                                                                |
| 1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a submission under 35 U.S.C. 371.<br>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a submission under 35 U.S.C. 371.<br>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.<br>4. <input type="checkbox"/> The US has been elected (Article 31).<br>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))<br>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).<br>b. <input checked="" type="checkbox"/> has been communicated by the International Bureau.<br>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).<br>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).<br>a. <input type="checkbox"/> is attached hereto.<br>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).<br>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))<br>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).<br>b. <input type="checkbox"/> have been communicated by the International Bureau.<br>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.<br>d. <input checked="" type="checkbox"/> have not been made and will not be made.<br>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).<br>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).<br>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).<br>Items 11 to 20 below concern document(s) or information included:<br>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.<br>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.<br>13. <input checked="" type="checkbox"/> A preliminary amendment.<br>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.<br>15. <input type="checkbox"/> A substitute specification.<br>16. <input type="checkbox"/> A power of attorney and/or change of address letter.<br>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.<br>18. <input checked="" type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).<br>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).<br>20. <input type="checkbox"/> Other items or information: |                                                         |                                                                                                                |

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

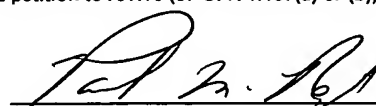
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PTO-1390 (Rev. 12-2004)

Approved for use through 3/31/2007. OMB 0651-0021

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            |                                                                                                                                                               |    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|-------------------------------------------------------------------------------|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| U.S. APPLICATION NO. (if known, see 37 CFR 1.5)<br><b>10/517686</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |              | INTERNATIONAL APPLICATION NO.<br>PCT/NL03/00422                               |            | ATTORNEY'S DOCKET NUMBER<br>0470-045923                                                                                                                       |    |
| 21. The following fees are submitted:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |                                                                               |            |                                                                                                                                                               |    |
| <input checked="" type="checkbox"/> a) Basic national fee.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                                                                               |            | \$ 300.00                                                                                                                                                     |    |
| <input checked="" type="checkbox"/> b) Examination fee.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               |            | \$ 200.00                                                                                                                                                     |    |
| <input checked="" type="checkbox"/> c) Search fee.....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |              |                                                                               |            | \$ 500.00                                                                                                                                                     |    |
| <b>TOTAL OF ABOVE CALCULATIONS =</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |              |                                                                               |            | <b>\$1000.00</b>                                                                                                                                              |    |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                                                                               |            |                                                                                                                                                               |    |
| Total Sheets                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Extra sheets | Number of each additional 50 or fraction thereof (round up to a whole number) |            | RATE                                                                                                                                                          |    |
| - 100 =                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | /50 =        |                                                                               |            | x \$250.00                                                                                                                                                    | \$ |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            | \$ 130.00                                                                                                                                                     |    |
| CLAIMS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NUMBER FILED | NUMBER EXTRA                                                                  | RATE       |                                                                                                                                                               | \$ |
| Total claims                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 16 - 20 =    | 0                                                                             | x \$50.00  |                                                                                                                                                               | \$ |
| Independent claims                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1 - 3 =      | 0                                                                             | x \$200.00 |                                                                                                                                                               | \$ |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               | + \$360.00 |                                                                                                                                                               | \$ |
| <b>TOTAL OF ABOVE CALCULATIONS =</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |              |                                                                               |            | <b>\$ 1,130.00</b>                                                                                                                                            |    |
| <input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            |                                                                                                                                                               |    |
| <b>SUBTOTAL =</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |              |                                                                               |            | <b>\$ 1,130.00</b>                                                                                                                                            |    |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |              |                                                                               |            | +                                                                                                                                                             | \$ |
| <b>TOTAL NATIONAL FEE =</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               |            | <b>\$</b>                                                                                                                                                     |    |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |              |                                                                               |            | +                                                                                                                                                             | \$ |
| <b>TOTAL FEES ENCLOSED =</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            | <b>\$ 1,130.00</b>                                                                                                                                            |    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            | Amount to be refunded:                                                                                                                                        | \$ |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            | Amount to be charged:                                                                                                                                         | \$ |
| <p>a. <input checked="" type="checkbox"/> A check in the amount of \$ 1,130.00 to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit t Account No. 23-0650. A duplicate copy of this sheet is enclosed.</p> <p>d. <input type="checkbox"/> Fees are to be charged to a credit card. <b>WARNING:</b> Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.</p> |              |                                                                               |            |                                                                                                                                                               |    |
| NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                                                                               |            |                                                                                                                                                               |    |
| SEND ALL CORRESPONDENCE TO:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               |            |                                                                                                                                                               |    |
| William H. Logsdon                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                                                                               |            |                                                                                                                                                               |    |
| Webb Ziesenheim Logsdon Orkin & Hanson, P.C.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            |                                                                                                                                                               |    |
| 436 Seventh Avenue                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                                                                               |            |                                                                                                                                                               |    |
| 700 Koppers Building                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |              |                                                                               |            |                                                                                                                                                               |    |
| Pittsburgh, PA 15219-1818                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |              |                                                                               |            |                                                                                                                                                               |    |
| Telephone: (412) 471-8815                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |              |                                                                               |            |                                                                                                                                                               |    |
| Facsimile: (412) 471-4094                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |              |                                                                               |            |                                                                                                                                                               |    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            | <br>SIGNATURE<br>Paul M. Reznick<br>NAME<br>33,059<br>REGISTRATION NUMBER |    |

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

ATTORNEY'S DOCKET NUMBER

Evert Johannes BUNSCHOTEN,  
Herman Jan Tijmen COELINGH BENNINK  
and Christian Franz HOLINKA

0470-045923

PCT/NL03/00422

ENTITLED

**"METHOD OF TREATING OR PREVENTING IMMUNE MEDIATED DISORDERS  
AND PHARMACEUTICAL FORMULATION FOR USE THEREIN"**

**To MAIL STOP PCT**

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Alexandria, VA 22313-1450

**EXPRESS MAIL CERTIFICATE**

"Express Mail" Label Number EV534973429US

Date of Deposit December 10, 2004

I hereby certify that the following attached papers or fees

**TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/  
ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER  
35 U.S.C. 371 (original and two (2) copies) and check in amount  
of \$1,130.00 for filing fee and surcharge fee for late Declaration  
LETTER RECOGNIZING ATTORNEYS (1 p.)  
PRELIMINARY AMENDMENT with ABSTRACT  
WO 03/103684 – FRONT PAGE with ABSTRACT, SPECIFICATION,  
CLAIMS and SEARCH REPORT (47 pp.)  
INTERNATIONAL PRELIMINARY EXAMINATION REPORT with ANNEX (8 pp.)**

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA, 22313-1450.

Nora Ann Pastrick

(Typed name of person mailing paper or fee)

*Nora Ann Pastrick*  
(Signature of person mailing paper or fee)